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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,335	08/15/2001	Graham Paul Matthews	4-30811A/C1	1679

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,335	MATTHEWS ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *10,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE) Under 37 CFR 1.114

1. Acknowledgment is made of applicant's filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.114.

2. Applicant's arguments with respect to claims 1-9 and 11 have been considered but are moot in view of the new ground(s) of rejection.

Claim Objections

3. Claim 9 is objected to because of the following informalities: Typographical error of "810% of a surfactant or surfactant mixture" is present in line 5 of claim 9. "810%" should be corrected as "80%".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claim 1-2, 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Weder et al. (EP 0733372 A2) or under 35 U.S.C. 102(e) as being anticipated by Weder et al. (US 5726164 A). It is noted that US 5726164 A is English equivalent to EP 0733372 A2.

Weder teaches a composition comprising N-benzoyl-staurosporin, a hydrophilic component (e.g., ethanol and water), surfactant such as polyoxyethylene/polyoxypropylene block copolymer (e.g., Pluronic F68 and Lutrol F68), lipophilic component such as phospholipids, in particular purified lecithin from soybeans (e.g., LIPOID S 100), and additives (e.g., glycerol and sorbitol), wherein said composition produces a suspension of colloidal nanoparticles (abstract; column 2, line 60 thru column 6, line 8; column 7, lines 40-42; Examples 1-3).

With respect to the claimed "HLB value" in claim 6, the referenced Pluronic F68 and soybean lecithin phospholipid, namely LIPOID S 100, must inherently possess the claimed properties and characteristics since the instant specification lists Pluronic F68 as the "surfactant of high HLB value, e.g., HLB > 10" (page 5, line 28; page 7, lines 28-31) and soya bean lecithins as the "surfactant having a low HLB value, e.g., HLB <10" (page 8, line 4 and page 10, lines 4-5). Therefore, the reference clearly anticipates the claimed invention.

Since the instant composition allows for the inclusion of any other unspecified ingredients even in major amounts, therefore, the referenced composition anticipates the claimed invention.

It is noted that applicant's statement of intended use or purpose such as "for oral administration" is limiting to the interpretation of composition claim. Therefore, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (EP 0733372 A2 or its English equivalent to US 5726164).

The teaching of Weder has been discussed in above 35 USC 102(b) or (e) rejection.

The teaching of Weder differs from the claimed invention in (i) the specific amounts active and inactive ingredients (claim 9) and (ii) "bioavailability levels of N-benzoylstaurosporine of from 5 to 17%", "AUC...of from 380 to 2000", and "Cmax...of from 60 to 310" (claim 11). However, those of ordinary skill in the art would have readily optimized effective dosages as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose or dosage having the desired bioavailability, AUC, and Cmax of the active ingredient may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage or the appropriate pharmacokinetic of N-enzoylstaurosporine for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed herein

6. Claims 5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (EP 0733372 A2 or its English equivalent to US 5726164) in view of Henry (US 5736542) and Weder et al. (US 5658898).

The teaching of Weder has been discussed in above 35 USC 102 (b) or (e) rejection.

Henry teaches the use of a transesterified ethoxylated vegetable oil (which is mixtures of mono, di and triglycerides and polyethylene glycol mono and diesters) in N-benzoylstaurosporine composition (column 1, line 44 thru column 2, line 9).

Weder'898 teaches a composition comprising N-benzoyl-staurosporine, a hydrophilic component (e.g., sorbitan, mannitol, glucose, lactose or fructose), purified lecithin from soybeans (e.g., LIPOIDS 100), a fatty acid tryglyceride (e.g., MIGLYOL 812) and polyoxyethylene sorbitan (e.g., TWEEN). See column 3, line 15 thru column 6, line 16; Claims 1-2.

The teaching of Weder'164 differs from the claimed invention in use of polysorbate and transesterified ethoxylated vegetable oil in said composition. To incorporate such teaching into the teaching of Weder'164, would have been obvious in view of Henry who teaches the use of a transesterified ethoxylated vegetable oil in N-benzoylstaurosporine composition and Weder'898 who teaches the use of polyoxyethylene sorbitan (e.g., TWEEN) in N-benzoylstaurosporine composition.

The above references in combination make clear that use of secondary agents such as polysorbate (e.g., TWEEN) and transesterified ethoxylated vegetable oil in preparing N-benzoylstaurosporine formulation (to improve the solubility of N-benzoylstaurosporine) is old and well known. The above references in combination make clear that the preparation of N-benozoylstaurosporine in various dosage forms including intravenous and oral are old and well known. One having ordinary skill in the art would have been motivated to make the claimed N-benzoylstaurosporine formulation containing all the ingredients herein (hydrophilic component (e.g., ethanol, polyethylene glycol), surfactants (e.g., polyoxyethylenes, polyalkylene oxide copolymers, polysorbate), lipophilic component (e.g., purified lecithin from soybeans, a fatty

acid tryglyceride) such that the bioavailability of N-benzoylstaurosporine would be significantly increased. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

6. No Claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614